REMARKS

Claims 84-141 are pending in the application. Claims 91-93, 105-108, 113-125, and 127-141 are withdrawn from consideration. Claims 85 and 90 have been canceled without prejudice or disclaimer. Claims 84, 86, 87, 89, 94-102, 104, 109, 110 and 126 have been amended to better clarify what Applicants believe to be the invention. Support for the amendments can be found throughout the specification, but particularly in the sequence listing as filed and in particular, in SEQ ID NOs: 1 and 2, for which the GenBank accession number is cited as L25119 in the specification on page 2, lines 31-32, and in SEQ ID NO: 3 (designated as T67C nucleotide sequence); SEQ ID NO: 4 (designated as T67C amino acid sequence); SEQ ID NO: 5 (designated as T124A nucleotide sequence); SEQ ID NO: 6 (designated as T124A amino acid sequence); SEQ ID NO: 7 (designated as C153T nucleotide sequence); SEQ ID NO: 8 (designated as G174A nucleotide sequence); SEQ ID NO: 9 (designated as 187INS:GGC nucleotide sequence) and SEQ ID NO: 10 (designated as 187INS:GGC amino acid sequence). Further support for the claim amendments can be found in Figure numbers: 1A, 1B, 2A, 2B, 3A, 3B, 4, 5, 6A and 6B and in the Brief Description of the Drawings on page 35, lines 5-23. Additional support for the claim amendments can be found on page 8, lines 30-31; page 9, lines 1-6; page 10, lines 30-31 and page 11, lines 1-5. Additional support can be found in the Examples on page 78, lines 25-31; page 79, lines 1-2; page 79, lines 21-31 and page 80, lines 1-5. No new matter has been entered by way of this amendment. Thus, as a result of the foregoing amendment, claims 84, 86-89, 94-104, 109-112 and 126 are under consideration.

Rejection under 35 U.S.C. §101

The Examiner has rejected claims 84, 87 and 89 under 35 U.S.C. §101 because they encompass non-statutory subject matter. More particularly, the Examiner alleges that the claims recite mutant alleles or nucleic acids encoding mutant polypeptides and do not contain language that indicates that the claimed molecules are isolated or in any way separated from the cells in which they would naturally be present. As the Examiner has noted, this rejection may be overcome by amendment of the claim to include the term "isolated" or "purified" nucleic acids.

Accordingly, and as suggested by the Examiner, the claims have been amended to include the term "isolated", thus obviating the Examiner's rejection under 35 U.S.C. 101. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner has also rejected claims 84-90, 94-104, 109-112 and 126 under 35 U.S.C. 112, second paragraph as being indefinite. More particularly, claim 84 is allegedly indefinite because it is not clear what is meant when applicant claims "a variant allele".

The Examiner notes that an allele is one of the different forms of a gene present in a particular nucleic acid sequence. Furthermore, the Examiner alleges that it is not clear from the language of claim 84, however, if by claiming an allele applicant is claiming a full length coding sequence with particular changes or if applicant is claiming fragments which overlap with polymorphic positions, etc.. The portion of the claim set forth after the transitional phrase "comprising" states that the claimed allele has "a DNA sequence having variation in SEQ ID NO: 1," however, the claim does not set forth how much variation is permitted, the claim merely sets forth that the variation must comprise at least those listed in the claim. The Examiner alleges that it is confusing as to what is being claimed, and what is encompassed within the claimed invention. Furthermore, the Examiner alleges that the nomenclature used to define the variation is also confusing and undefined, and that neither the claims nor the specification define what is meant by the nomenclature, for example "T124A". The claim appears to imply that the variation would be within SEQ ID NO: 1, at position 124, but turning to SEQ ID NO: 1, and counting to the 124th position, the Examiner notes that there is guanine at this position, so it is confusing what is meant by this nomenclature. The Examiner notes that the claims would be immensely clarified if the location of the polymorphisms were given in some specific context. The Examiner has suggested claim language which would overcome all of the preceding issues under 112 2nd paragraph. For example:

"An isolated nucleic acid wherein said nucleic acid comprises the DNA sequence of SEQ ID NO: 1, except that one or more of the following variations are present:

(a) the "T" at position 279 of SEQ ID NO: 1 is replaced with a "C";

(b) the "T" at position 336 of SEQ ID NO: 1 is replaced with an "A";

(c) the "C" at position 365 of SEQ ID NO: 1 is replaced with a "T";

(d) the "G" at position 386 of SEQ ID NO: 1 is replaced with an "A";

(e) the nucleotides "GGC" are inserted following position 401 of SEQ ID NO: 1."

The Examine further notes that all claims which depend from claim 84 are indefinite for these same reasons.

The Examiner alleges that claim 89 is similarly indefinite because the metes and bounds of this claim are unclear. Like claim 84, claim 89 is indefinite because it is not clear what is meant when applicant claims "a variant allele". The claim sets forth that the claimed allele encodes a receptor comprising "an amino acid sequence having a variation in SEQ ID NO: 2" however, the claim does not set forth how much variation is permitted, nor how much of SEQ ID NO: 2 is required to be present in the claimed allele.

Furthermore, the nomenclature used to define the variation is also confusing and undefined. The claim requires that the variation "comprise" Ser23Pro, but does not define what this nomenclature means, nor does the specification define the nomenclature. The definition of the variation does not particularly refer to SEQ ID NO: 2, and since it is not clear from the preceding language of the claim how much of SEQ ID NO: 2 is required to be encoded by the claimed "variant allele". Claim 90 is indefinite for these reasons as it depends from claim 89.

The Examiner alleges that claim 104 is indefinite for similar reasons as claim 89. In addition, claim 126 is also indefinite for reasons as discussed for claim 84.

Applicants respectfully traverse the Examiner's rejection and have amended the claims as suggested by the Examiner to place the application in condition for allowance. More particularly, claim number 84 has been amended to recite:

"An isolated nucleic acid, wherein said nucleic acid comprises the DNA sequence of SEQ ID NO:1, except that one or more of the following variations are present:

a) the "T" at position 279 of SEQ ID NO: 1 is replaced with a "C";

b) the "T" at position 336 of SEQ ID NO: 1 is replaced with an "A";.

c) the "C" at position 365 of SEQ ID NO: 1 is replaced with a "T";

d) the "G" at position 386 of SEQ ID NO: 1 is replaced with an "A";

e) the nucleotides "GGC" are inserted following position 401 of SEQ ID NO: 1."

Likewise, claim 89 has been amended to recite:

"An isolated nucleic acid encoding a human mu opioid receptor variant, wherein said variant comprises an amino acid sequence having one or more of the following variations in SEQ ID NO: 2:

a) the serine at position 23 of SEQ ID NO: 2 is replaced with a proline;

b) the serine at position 42 of SEQ ID NO: 2 is replaced with a threonine;

c) the addition of a glycine residue following the glycine at position 63."

In addition, claims 100, 102, 104, 109, 110 and 126 have been amended in a similar fashion to better clarify the invention.

Based on the foregoing amendments, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. §112, first paragraph

Claims 84-90, 94-104, 109-112 and 126 are rejected under 35 U.S.C. 112, first paragraph is failing to comply with the written description requirement. The claims are drawn to variant alleles of human mu opioid receptor genes as well as molecules that "selectively hybridize" to the same, as well as a kit comprising primers for the detection of the same. In addition to being indefinite, the claims also lack written description because as they are written, the claims require very little structural elements. In addition, the claims as written do not require that the encoded receptor have any particular function, nor do they have any particular core sequence. Neither the claims nor the specification discuss what is necessary and essential for a sequence to be "a variant allele of a human mu opioid receptor gene," that is, though the claims are permissive of any level of variation from SEQ ID NO: 1, there is no guidance as to how to identify which variants of SEQ ID NO: 1 are actually alleles of a human mu opioid receptor gene. More particularly, the Examiner alleges that the claims are extremely broad. Further, many of the claims do not even require the variant alleles, but only require sequences that are "selectively hybridizable" to the variant alleles, and these claims are even broader in nature since they encompass any molecule that would hybridize to the mutant alleles, including sequences from other mammals, or other organisms with mu opioid receptors, as well as fragments of SEQ ID NO: 1 itself.

The Examiner alleges that within this extremely broad genus of claims, applicant has provided only a limited number of examples. Applicants have taught that the known human mu opioid receptor is represented by SEQ ID NO: 1, and they have taught five novel variations of this sequence, namely (a) the "T" at position 279 of SEQ ID NO: 1 is replaced with a "C"; (b) the "T" at position 336 of SEQ ID NO: 1 is replaced with an "A"; (c) the "C" at position 365 of SEQ ID NO: 1 is replaced with a "T"; (d) the "G" at position 386 of SEQ ID NO: 1 is replaced with an "A"; and (e) the nucleotides "GGC"are inserted following position 401 of SEQ ID NO: 1. The Examiner alleges that the claims however, encompass any number of additional variations with SEQ ID NO: 1, including any number of substitutions, deletions, inversions, insertions, and the like. The molecules provided in the specification are not representative of this broad genus because they represent only very small and specific changes to instant SEQ ID NO: 1, while the instant claims encompass, literally a change at any nucleotide within the sequence. The Examiner notes that this rejection may be overcome by amending the claims to recite the specific variants for which we have support.

Applicants respectfully traverse the Examiner's rejection and have amended the claims to recite the specific variants for which support is provided in order to move the application along to allowance. The amended claim language has been provided above for claim numbers 84 and 89. Similar amendments have been made to claim numbers 100, 102, 104, 109, 110 and 126, as noted above. Accordingly, these claims and the claims dependent from these claims have all been amended as suggested by the Examiner, and as such, withdrawal of the rejection under 35 U.S.C. 112, first paragraph is respectfully requested.

Rejection under 35 U.S.C. §102(b)

The Yu reference

Claims 84-90, 94-104 and 109-112 are rejected under 35 U.S.C. 102(b) as being anticipated by Yu (WO 95/07983).

In particular, Yu teaches a human mu opioid receptor gene comprising a DNA sequence having a variation in SEQ ID NO: 1, wherein said variation comprises an "A" at position 124 and a "T" at position 153. Yu teaches that their SEQ ID NO: 7 encodes a human mu opioid receptor and has a variation relative to SEQ ID NO: 1, for example, the first ten nucleotides of

the two sequences. Since the sequence taught by Yu has an "A" at position 124 and a "T" at position 153, it appears to comprise a variation as required by claim 84.

The Examiner further notes that with regard to claim 85, Yu specifically teaches "isolated and purified polynucleotides" including an isolated and purified polynucleotide comprising SEQ ID NO: 7 (p. 10, lines 12-15). With regard to claim 86, Yu teaches labels attached to the polynucleotides of the claimed invention (p. 36, line 35). With regard to claim 87, Yu teaches probes and primers that are fragments of their SEQ ID NO: 7, and these would all selectively hybridize to the variant that they teach (p. 32-37). With regard to claim 88, Yu teaches a label on the probes and primers (p. 36, line 35). Further, with regard to claim 87, Yu teaches the use of the rat mu opioid receptor cDNA to hybridize to and detect the human sequence. With regard to claim 89, the claim is broadly drawn to require only that the claimed allele encode a variant which comprises "an" amino acid sequence having a variation in SEQ ID NO: 2, and this could be any fragment of SEQ ID NO: 2 which comprises the variations listed in the claim. The variant allele taught by Yu encodes at least a Gly-Gly fragment (see 53-54 of encoded SEQ ID NO: 8). Thus, the Examiner alleges that the gene taught by Yu encodes a receptor comprising "an" amino acid sequence having a variation in SEQ ID NO: 2 which is the addition of Gly following another Gly. Since the claim does not specifically and clearly set forth how much of SEQ ID NO: 2 is required and the claim does not specifically provide context for the recitation "Gly 63" the claim is interpreted as encompassing the molecule set forth by Yu. With regard to claim 90, Yu specifically teaches "isolated and purified polynucleotides" including an isolated and purified polynucleotide comprising SEQ ID NO: 7 (p. 10, lines 12-15). With regard to claims 94, 95, 96 and 97, Yu teaches a cloning or expression vector comprising SEQ ID NO: 7 and an origin of replication. Namely, Yu specifically teaches that the cDNA was cloned downstream of the human CMV promoter in a mammalian expression vector (p. 108, lines 15-18). Further with respect to claim 97, Yu teaches the rat mu opioid receptor gene with an expression vector, and as previously discussed in this rejection, the rate gene is "selectively hybridizable" to the human variant (p. 99). With respect to claims 98 and 99, Yu teaches unicellular host cells transformed or transfected with an expression vector (see p. 108 and p. 99). With respect to claims 100,102, 109 and 110, the nucleic acid taught by Yu has an "A" at position 124 and a "T" at position 153, thus it appears to comprise two variations as required by the claim. Further, with regard to 102 and 110, Yu teaches the use of the rat mu opioid receptor

cDNA to hybridize to and detect the human sequence. With regard to claims 101 and 103, as previously discussed, Yu teaches labeled molecules. With regard to claim 104, Yu teaches a molecule that encodes a receptor comprising "an amino acid sequence" having all of the variations required, where the claim is interpreted to require only a proline, a threonine, and a glycine following a glycine. With respect to claim 105, the nucleic acid taught by Yu has an "A" at position 124 and a "T" at position 153, thus it has and would hybridize to molecules with this variation. Further, with regard to 102, Yu teaches the use of the rat mu opioid receptor cDNA to hybridize to and detect the human sequence. Thus, the rat sequence probe used by Yu was "selectively hybridizable" to the human sequence since it was used in a hybridization to select the human sequence. With regard to claim 109, 110, 111 and 112, Yu teaches the sequence within vectors and the vectors within host cells, as previously discussed in this office action.

Applicants respectfully traverse the Examiner's rejection and have amended the claims cited in the rejection, in particular, claims 84, 86-89, 94-102, 104, and 109-110 to better clarify where the polymorphisms lie in relation to SEQ ID NO: 1. As noted in the amended claims, the variants as now claimed, are identified as having one or more of the following variations:

(a) the "T" at position 279 of SEQ ID NO: 1 is replaced with a "C";

(b) the "T" at position 336 of SEQ ID NO: 1 is replaced with an "A";

(c) the "C" at position 365 of SEQ ID NO: 1 is replaced with a "T";

(d) the "G" at position 386 of SEQ ID NO: 1 is replaced with an "A";

(e) the nucleotides "GGC" are inserted following position 401 of SEQ ID NO: 1."

More particularly, as the Examiner previously noted in the rejection under 35 U.S.C. 112, second paragraph, the nomenclature used to define the variation is confusing and undefined, and that neither the claims nor the specification define what is meant by the nomenclature, for example "T124A". The Examiner further noted that the claim appears to imply that the variation would be within SEQ ID NO: 1, at position 124, but turning to SEQ ID NO: 1, and counting to the 124th position, the Examiner notes that there is guanine at this position, so it is confusing what is meant by this nomenclature. The Examiner notes that the claims would be immensely clarified if the location of the polymorphisms were given in some specific context. Applicants accordingly have clarified the location of the polymorphisms by denoting the exact position in SEQ ID NO: 1 where the changes occur. By amending the claims of the present invention to better clarify the position of the polymorphisms identified by the Applicants, Applicants assert

that the sequences disclosed by Yu et al. no longer anticipate the claimed invention. That is, Yu et al do not teach or suggest the polymorphisms of the mμ opioid receptors as currently claimed in the instant invention. Withdrawal of the rejection is respectfully requested.

The Brennan reference

Claims 84, 85, 87, 89, 100, 102, 104 and 105 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (U.S. 5,474,796).

In particular, Brennan teaches an array that has every possible oligonucleotide of ten nucleotides, each as an isolated nucleic acid at a different position on the array (see Example 3, Col. 9). Since Brennan provides every possible combination of ten nucleotide probes on the array, Brennan teaches every possible variation within a fragment of our SEQ ID NO: 1 or any other context. This rejection applies to the claims that require that the allele has "at least two variations" because the claim does not require any context for the variation. Thus, the claim is broadly interpreted as requiring only that particular nucleotides or encoded polypeptides are present in the sequence.

Applicants respectfully traverse the Examiner's rejection for the reasons noted above. More particularly, Applicants have amended the claims to recite exactly where the polymorphisms lie as related to SEQ ID NO: 1. More particularly, claims 84, 87, 89, 100, 102, and 104 have been amended to include the specific regions of SEQ ID NO: 1 wherein the changes occur in the variants. Based on these claim amendments, Applicants assert that Brennan does not anticipate the polymorphisms as currently claimed. Furthermore, Applicants assert that Brennan does not teach or suggest the polymorphisms disclosed and as currently claimed in the present invention.

Claim 85 has been canceled without prejudice or disclaimer and claim 105 has been withdrawn from consideration, and as such, the rejection of these claims is moot.

The Bond reference

Claims 87, 102 and 105 are rejected under 35 U.S.C. 102(b) as being anticipated by Bond, *et al.* (PNAS U.S.A. Vol. 95, p. 9608-9613, August 1998).

In particular, the Examiner alleges that each of the rejected claims require a nucleic acid molecule that is selectively hybridizable to a variant human mu opioid receptor gene. The claims

do not, however, as originally filed, require that the claimed molecules contain any particular sequence or overlap with a sequence, therefore, any sequence that would selectively hybridize to any portion of a variant human mu opioid receptor gene is within the scope of these claims.

Moreover, the Examiner alleges that Bond, *et al.* teach primers for the amplification of the exons of the gene encoding human mu opioid receptors (p. 9609, 2nd column). These primers would selectively hybridize to isolated variant alleles of the human mu opioid receptor gene since they would hybridize to the gene for the amplification of the exons. This is considered "selectively hybridizing" because it is selective of the human mu opioid gene rather than other possible gene exons in a sample.

Applicants respectfully traverse the Examiner's rejection on the basis of the current claim amendments and for the reasons noted above. More particularly, Applicants have amended the claims to recite exactly where the polymorphisms lie as related to SEQ ID NO: 1.

For example, claim 87 has been amended to recite:

"An isolated nucleic acid molecule selectively hybridizable to the isolated nucleic acid of Claim 84, wherein the nucleic acid has at least two variations in SEQ ID NO:1 and wherein the at least two variations are selected from:

a) the "T" at position 279 of SEQ ID NO: 1 is replaced with a "C";

b) the "T" at position 336 of SEQ ID NO: 1 is replaced with an "A";.

c) the "C" at position 365 of SEQ ID NO: 1 is replaced with a "T";

d) the "G" at position 386 of SEQ ID NO: 1 is replaced with an "A"; and

e) the nucleotides "GGC" are inserted following position 401 of SEQ ID NO: 1, and wherein said isolated nucleic acid selectively hybridizes to one or more of the variations or the complement thereof."

Furthermore, claim 102 has been amended to recite:

"An isolated nucleic acid molecule selectively hybridizable to an isolated nucleic acid encoding a human mu opioid receptor variant comprising the DNA sequence of claim 84, except that the variant has at least two variations in SEQ ID NO:1 and wherein the at least two variations are selected from:

a) the "T" at position 279 of SEQ ID NO: 1 is replaced with a "C";

b) the "T" at position 336 of SEQ ID NO: 1 is replaced with an "A";.

c) the "C" at position 365 of SEQ ID NO: 1 is replaced with a "T";

d) the "G" at position 386 of SEQ ID NO: 1 is replaced with an "A"; and

e) the nucleotides "GGC" are inserted following position 401 of SEQ ID NO: 1, and wherein said isolated nucleic acid selectively hybridizes to one or more of the variations or the complement thereof."

Based on these claim amendments, Applicants assert that Bond does not anticipate primers that are selectively hybridizable to the polymorphisms as currently claimed. More particularly, Applicants specify exactly where the changes occur in the mμ opioid receptor variants. Applicants assert that Brennan does not teach or suggest these variants, nor primers that will selectively hybridize with these variants.

Moreover, the term "selectively hybridizable" as taught by the instant invention on page 42, lines 8-15, refers to polynucleotides capable of discriminating between the wild-type and polymorphic alleles of the invention. Claims 87 and 102 have been amended to recite the specific polymorphisms and note that the claimed nucleic acids must selectively hybridize to the variants or complement thereof. Applicants assert that Bond et al. do not teach or suggest the specific polymorphisms claimed in the present application, nor do Bond et al. teach or suggest nucleic acids that are selectively hybridizable to the variants as currently claimed.

Claim 105 has been withdrawn from consideration, and as such, the rejection is moot. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. §103(a)

Claim 126 is rejected under 35 U.S.C. §103(a) as being unpatentable over Bond, *et al.* (PNAS U.S.A., Vol. 95, p. 9608-9613, August 1998) in view of Ahern (The Scientist, Vol. 9, No. 15, page 20, July 1995).

In particular, the Examiner alleges that Bond, *et al.* teach primers for the amplification of the exons of the gene encoding human mu opioid receptors (p. 9609, 2nd column). These are PCR oligonucleotide primers suitable for detection of an allele comprising a human mu opioid receptor gene having any of the recited variations, since one could amplify using these primers and then undertake further analysis to determine the actual nucleotides present. The Examiner

further alleges that the claim does not require that the primers overlap with the variations, only that they are "suitable" for detection of an allele. These primers meet those limitations. Bond, *et al.* also teach "other reagents" such as an agarose gel (p. 9609, 2nd column).

Bond, *et al.* do not teach the packaging of these components into a kit which includes instructions.

Ahern provides a discussion of biochemical reagents kits, and teaches specifically that these "offer scientists good return on investment (title)". Ahern teaches there are many advantages to the purchase of biochemical kits, including that buying kits of premade reagents are convenient and save time, and that they include instructions (p. 4, second para). Thus, the Examiner alleges that at the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to have packaged the reagents taught by Bond, *et al.* into a kit including instructions for use so as to have provided a kit with the advantages expressly discussed by Ahern.

The Examiner has the initial burden of establishing a *prima facie* case of obviousness. A finding of obviousness under § 103 requires a determination of the scope and content of the prior art, the differences between the claimed invention and the prior art, the level of ordinary skill in the art, and whether the differences are such that the claimed subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. Graham v. Deere, 383 US 1 (1966). Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion that the combination be made. In re Stencel, 828 F2d 751, 4 USPQ2d 1071 (Fed. Cir. 1987). Furthermore, there must be a reasonable expectation of success for a rejection under § 103 to be proper.

The invention as claimed. The invention, as currently claimed relates to a commercial test kit for determining the presence of at least one variation in a human mu opioid receptor gene in a bodily sample taken from a subject, wherein the commercial test kit comprises:

a) PCR oligonucleotide primers capable of selectively hybridizing with a nucleic acid encoding a human mu opioid receptor variant comprising the DNA sequence of SEQ ID NO:1 except that one or more of the following variations are present:

i) the "T" at position 279 of SEQ ID NO: 1 is replaced with a "C";

ii) the "T" at position 336 of SEQ ID NO: 1 is replaced with an "A";.

iii) the "C" at position 365 of SEQ ID NO: 1 is replaced with a "T";

iv) the "G" at position 386 of SEQ ID NO: 1 is replaced with an "A";

v) the nucleotides "GGC" are inserted following position 401 of SEQ ID NO: 1;

b) other reagents; and

c) directions for use of the kit.

The Bond reference

As noted above by the Examiner, Bond, *et al.* teach primers for the amplification of the exons of the gene encoding human mu opioid receptors. These are PCR oligonucleotide primers suitable for detection of an allele comprising a human mu opioid receptor gene having any of the recited variations, since one could amplify using these primers and then undertake further analysis to determine the actual nucleotides present. Bond, *et al.* also teach "other reagents" such as an agarose gel (p. 9609, 2nd column).

Bond, *et al.* do not teach the packaging of these components into a kit which includes instructions.

The Examiner alleges that the claim as originally filed, does not require that the primers overlap with the variations, only that they are "suitable" for detection of an allele.

Applicants have amended the claims as suggested by the Examiner to better clarify where the changes occur in the nucleic acid sequences as related to SEQ ID NO: 1. As such, the claims as amended now recite where these changes occur in the specific variants. Furthermore, Applicants assert that Bond et al. do not teach or suggest the components of the kit as currently claimed, since these variants were not known to Bond et al. More particularly, as noted above, Bond et al. do not teach primers that are capable of selectively hybridizing with the variant nucleic acids of SEQ ID NO: 1, as currently claimed. As such, one skilled in the art would not be motivated to prepare a kit without knowing which primers would be suitable to allow for selective hybridization to the nucleic acid sequences or variants identified by the Applicants.

The Ahern reference

As noted above, Ahern provides a discussion of biochemical reagents kits, and teaches specifically that these "offer scientists good return on investment (title)". Ahern teaches there are many advantages to the purchase of biochemical kits, including that buying kits of premade reagents are convenient and save time, and that they include instructions.

The Examiner alleges that at the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to have packaged the reagents taught by Bond, *et al.* into a kit including instructions for use so as to have provided a kit with the advantages expressly discussed by Ahern.

Applicants respectfully traverse the Examiner's rejection based on the current claim amendments noted above. Without the proper teachings of the variant sequences, one could not prepare the proper primers to include with the reagents of the kit. Accordingly, the teachings of Ahern could not be combined with the teachings of Bond et al, since Bond et al. do not teach or suggest primers that would selectively hybridize with the mu opioid variants as currently claimed. Accordingly, Applicants assert that one skilled in the art could not prepare a kit even given the teachings of Ahern. The teachings necessary to practice the current invention were not provided by Bond or Ahern, and as such, Applicants assert that the rejection is moot.

Withdrawal of the rejection is respectfully requested.

Fees

No fees are believed to be necessitated by the instant response. However, should this be erroneous, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or credit any overages.

Conclusion

Applicants believe that the foregoing amendments to the claims place the application in condition for allowance. Withdrawal of the rejections is respectfully requested. If a discussion with the undersigned will be of assistance in resolving any remaining issues, the Examiner is invited to telephone the undersigned at (201) 487-5800, ext. 118, to effect a resolution.

Respectfully submitted,

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